

WHAT IS CLAIMED IS:

1. A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:
 - 5 contacting mutant hippocampal cells having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;
 - subjecting said mutant cells to tetanic stimulation; and
 - 10 determining the effect of said ^{candidate drug} ~~agent~~ on the synaptic potentiation of said mutant hippocampal cells;
 - 10 wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.
2. A method according to Claim 1, wherein said mutant cells are mutated in a
 - 15 presenilin gene.
3. A method according to Claim 2, wherein said mutant cells are mouse hippocampal tissue slices.
- 20 4. A method according to Claim 1, wherein said enhanced synaptic potentiation is as a result of a change in the GABA_A receptor pathway.
5. A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:
 - 25 contacting mutant hippocampal cells, having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells, with a candidate drug;
 - subjecting said mutant and wild-type hippocampal cells to a tetanic stimulus;
 - measuring changes in potentiation with time of the mutant and wild-type
 - 30 hippocampal cells and comparing the effect of said agent on the synaptic potentiation of said mutant as compared to the observed synaptic potentiation of said wild-type hippocampal cells;

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wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells as compared to the synaptic potentiation of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

5 6. A method according to Claim 5, including the additional steps of:

contacting mutant hippocampal cells having enhanced synaptic potentiation upon tetanic stimulation as compared to wild-type hippocampal cells with a GABA_A receptor antagonist;

subjecting said mutant and wild-type hippocampal cells to tetanic stimulation;

10 and

measuring changes in synaptic potentiation with time of the mutant and wild-type hippocampal cells and comparing the effect of said GABA_A receptor antagonist on said mutant and said wild-type hippocampal cells;

wherein a reduction in the enhanced synaptic potentiation of the mutant

15 hippocampal cells without a ^{statistically} significant change in the synaptic potentiation of the wild-type cells is indicative of the mutation acting on a common pathway with said GABA_A receptor antagonist.

7. A method according to Claim 5, wherein said agent is present with said wild-
20 type hippocampal cells.

8. A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:

25 contacting mutant hippocampal cells having enhanced synaptic potentiation upon stimulation as compared to wild-type hippocampal cells with a candidate drug;

subjecting said mutant and wild-type hippocampal cells to a tetanic stimulus at a first potential of glutamate currents and a second potential of GABA_A currents;

30 measuring the synaptic response at each of the first and second potentials for the mutant and wild-type hippocampal cells and comparing the effect of said agent on said mutant and said wild-type hippocampal cells;

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wherein a reduction in the enhanced synaptic response of the mutant hippocampal cells without a ^{statistically} significant change in the synaptic response of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

- 5 9. A method for screening for drugs for the treatment of Alzheimer's disease, said method comprising:

contacting mutant mouse hippocampal cells mutated in the presenilin-1 gene and having enhanced synaptic potentiation upon tetanic stimulation as compared to wild-type hippocampal cells with a candidate drug;

- 10 subjecting said mutant and wild-type hippocampal cells to tetanic stimulation; and

comparing the effect of said agent on said mutant and said wild-type hippocampal cells upon tetanic stimulation;

- wherein a reduction in the enhanced synaptic potentiation of the mutant hippocampal cells without a ^{statistically} significant change in the synaptic potentiation of the wild-type cells is indicative of activity of a candidate drug for the treatment of Alzheimer's disease.

10. Slices of mouse hippocampal cells having a mutation in a presenilin gene
20 combined with a candidate drug.

11. Slices of mouse hippocampal cells according to Claim 10, after tetanic stimulation.

- 25 12. Slices of mouse hippocampal cells according to Claim 10, wherein said mutation is the PS-1 $\Delta 9$ mutation.